Paper No. 26

UNITED STATES PATENT AND TRADEMARK OFFICE

BEFORE THE BOARD OF PATENT APPEALS AND INTERFERENCES

Ex parte VICTOR M. GOLDBERG, ARNOLD I. CAPLAN, FRANCIS P. BARRY, DAVID J. FINK, DANIEL R. MARSHAK, and JAMES S. BURNS

Appeal No. 2003-0837
Application No. 09/078,531

ON BRIEF

Before SCHEINER, ADAMS, and MILLS, Administrative Patent Judges.

ADAMS, Administrative Patent Judge.

DECISION ON APPEAL

This is a decision on the appeal under 35 U.S.C. § 134 from the examiner's final rejection of claims 33-51, which are all the claims pending in the application.

Claim 33 is illustrative of the subject matter on appeal and is reproduced below:

> 33. A method for regenerating articular cartilage defects in a host in need thereof, comprising administering to said host cultured human mesenchymal stem cells, said human mesenchymal stem cells having a fibroblastic morphology.

The references relied upon by the examiner are:

Nevo et al. (Nevo)	4,642,120	Feb. 10, 1987
Itay	5,053,050	Oct. 1, 1991
Bruder et al. (Bruder)	5,736,396	Apr. 7, 1998
Grande et al. (Grande)	5,906,934	May 25, 1999

Pettipher et al. (Pettipher), "Interleukin 1 induces leukocyte infiltration and cartilage proteoglycan degradation in the synovial joint," Proc. Natl. Acad. Sci., Vol. 83, pp. 8749-53 (1986)

Joyce et al. (Joyce), "Transforming Growth Factor-b and the Initiation of Chondrogenesis and Osteogenesis in the Rat Femur," J. Cell Biology, Vol. 110, pp. 2195-207 (1990)

GROUNDS OF REJECTION

Claims 33-35, 40, 41, 43, 44, 47-49, 50 and 51 stand rejected under 35 U.S.C. § 102(e) as being anticipated by or, in the alternative, under 35 U.S.C. § 103 as being obvious over Grande.

Claims 42, 45 and 46 stand rejected under 35 U.S.C. 102(e) as anticipated by or, in the alternative, under 35 U.S.C. 103 as obvious over Grande.

Claims 36 and 37 stand rejected under 35 U.S.C. § 103 as being unpatentable over Grande in view of Joyce and Bruder.

Claim 38 is rejected under 35 U.S.C. § 103 as being unpatentable over Grande in view of Bruder and Pettipher.

Claim 39 is rejected under 35 U.S.C. § 103 as being unpatentable over Grande in view of Nevo and Itay.

We reverse.

DISCUSSION

THE REJECTIONS UNDER 35 U.S.C. § 102(e)/103:

Claims 33-35, 40, 41, 43, 44, 47-49, 50 and 51

According to the examiner (Answer, page 3), "[o]ther than the phrase describing the mesenchymal stem cells as explicitly being human and as 'having a fibroblastic morphology', all other limitations of the cited claims are clearly anticipated by the Grande et al. patent." To make up for this deficiency, the examiner finds (id.), Grande "discloses at col. 3, lines 61-62 that 'MSC's can be obtained from bone marrow or other mesenchymal tissues.'" For the sake of clarity, the cited section of Grande states, mesenchymal stem cells (MSCs) "are preferably isolated from muscle using a standard punch or dermal biopsy. However, MSCs can be obtained from bone marrow or other mesenchymal tissues." The examiner also finds (id.), Grande discloses "at col. 3, lines 66-67 … that mammalian MSCs are contemplated for use in the practice of this invention. Implicit in this statement is the inherent disclosure of human as well as all other mammalian MSCs." To be clear, Grande disclose (column 3, lines 63-67), "[a] detailed procedure for isolation of MSCs from embryonic chick muscle is described by Young…. The same basic procedure is used for isolation of mammalian MSCs from muscle."

According to the examiner (Answer, bridging sentence, pages 3-4), column 2, line 63 of Grande refers to Caplan, United States Patent 5,226,914, and is cited as disclosing mesenchymal stem cells used in the process of stimulating bone formation. Appellants agree with the examiner's

characterization of Grande's citation to Caplan. Brief, page 4. Appellants, however, point out (Brief, pages 3 and 4), Grande disclose mesenchymal stem cells as having a characteristic mononuclear, stellate shape (see Grande, column 9, lines 50-54), not a fibroblastic morphology as required by appellants' claimed invention.

To bridge this difference in morphology, the examiner directs our attention to the disclosure at column 11, lines 47-50 of Caplan. According to the examiner (Answer, page 4), column 11, lines 47-50 of Caplan "discloses human mesenchymal stem cells obtained from bone marrow as having 'similar morphology, almost all being fibroblastic, with few adipocytic, polygonal or round cells.[']" Once again, for clarity we note that the cited section of Caplan states (column 11, lines 47-40), "[a]dherent marrow-derived mesenchymal stem cells derived from femoral head cancellous bone or iliac aspirate have similar morphology, almost all being fibroblastic, with few adipocytic, polygonal or round cells."

As we understand the examiner's position, Grande teaches the claimed invention but for human mesenchymal stem cells having a fibroblastic morphology. To make up for the deficiency in Grande, the examiner relies upon what the examiner characterizes (Answer, pages 3-4), as a number of "implicit statements" and "inherent disclosures" in the Grande disclosure.

First, the examiner selects bone marrow from Grande's disclosure that mesenchymal stem cells (MSCs) "are preferably isolated from muscle using a

standard punch or dermal biopsy. However, MSCs can be obtained from bone marrow or other mesenchymal tissues."

Then, notwithstanding Grande's use of mesenchymal stem cells obtained from rabbit muscle (see Brief, page 3), the examiner selects humans from Grande's disclosure that "[a] detailed procedure for isolation of MSCs from embryonic chick muscle is described by Young…. The same basic procedure is used for isolation of mammalian MSCs from muscle."

Finally, using Grande's reference to Caplan as a foot-hold, the examiner relies on Caplan's disclosure that "[a]dherent marrow-derived mesenchymal stem cells derived from femoral head cancellous bone or iliac aspirate have similar morphology, almost all being fibroblastic, with few adipocytic, polygonal or round cells."

Based on this analysis, the examiner finds (Answer, page 4), "marrow-derived human mesenchymal stem cells inherently have 'a fibroblastic morphology' and that this property would be inherently found in the mesenchymal stem cells of the Grande et al. patent, since Grande explicitly teaches the obtention [sic] of mesenchymal stem cells from bone marrow, thereby anticipating the cited claims."

The examiner's analysis begs the question, besides appellants' claimed invention, what is directing the examiner's selection of human bone marrow, from the disclosure of Grande? Furthermore, assuming arguendo Grande does direct a person of ordinary skill in the art to human bone marrow, why does Grande necessarily lead one to bone marrow from femoral head cancellous bone or iliac

aspirate? Notwithstanding the examiner's statement that marrow-derived human mesenchymal stem cells inherently have a fibroblastic morphology, it has only been demonstrated that adherent marrow-derived mesenchymal stem cells derived from femoral head cancellous bone or iliac aspirate have a fibroblast-like morphology.

We recognize that when an anticipatory reference is silent with regard to an asserted inherent characteristic, the gap in the reference may be filled with by reference to extrinsic evidence. However, the extrinsic "evidence must make clear that the missing descriptive matter is necessarily present in the thing described in the reference, and that it would be so recognized by persons of ordinary skill." Continental Can Co. USA Inc. v. Monsanto Co., 948 F.2d 1264, 1268, 20 USPQ2d 1746, 1749 (Fed. Cir. 1991). The examiner appears to recognize (Answer, page 12), as set forth in In re Robertson, 169 F.3d 743, 745, 49 USPQ2d 1949, 1950-51 (Fed. Cir. 1999):

> If the prior art reference does not expressly set forth a particular element of the claim, that reference still may anticipate if that element is "inherent" in its disclosure. To establish inherency, the extrinsic evidence "must make clear that the missing descriptive matter is necessarily present in the thing described in the reference, and that it would be so recognized by persons of ordinary skill." Continental Can Co. v. Monsanto Co., 948 F.2d 1264, 1268, 20 U.S.P.Q.2d 1746, 1749 (Fed. Cir. 1991). "Inherency, however, may not be established by probabilities or possibilities. The mere fact that a certain thing may result from a given set of circumstances is not sufficient." Id. at 1269, 20 U.S.P.Q.2d at 1749 (quoting In re Oelrich, 666 F.2d 578, 581, 212 U.S.P.Q. 323, 326 (C.C.P.A. 1981).

On this record, the examiner has made very specific selections from the genus of options set forth in Grande. In our opinion, this picking and choosing

not sufficient to establish a prima facie case of anticipation. When the claimed invention is not identically disclosed in a reference, and instead requires picking and choosing among a number of different options disclosed by the reference, then the reference does not anticipate. Akzo N.V. v. International Trade Commission, 808 F.2d 1471, 1480, 1 USPQ2d 1241, 1245-46 (Fed. Cir. 1986); In re Arkley, 455 F.2d 586, 587-88, 172 USPQ 524, 526 (CCPA 1972). Accordingly, it is our opinion that the examiner failed to meet her burden of establishing a prima facie case of anticipation.

Similarly, it is our opinion that the examiner failed to meet her burden of establishing a prima facie case of obviousness. As set forth in In re Kotzab, 217 F.3d 1365, 1369-70, 55 USPQ2d 1313, 1316 (Fed. Cir. 2000):

> A critical step in analyzing the patentability of claims pursuant to section 103(a) is casting the mind back to the time of invention, to consider the thinking of one of ordinary skill in the art, guided only by the prior art references and the then-accepted wisdom in the field. … Close adherence to this methodology is especially important in cases where the very ease with which the invention can be understood may prompt one "to fall victim to the insidious effect of a hindsight syndrome wherein that which only the invention taught is used against its teacher."
>
> …
>
> Most if not all inventions arise from a combination of old elements. … Thus, every element of a claimed invention may often be found in the prior art. … However, identification in the prior art of each individual part claimed is insufficient to defeat patentability of the whole claimed invention. … Rather, to establish obviousness based on a combination of the elements disclosed in the prior art, there must be some motivation, suggestion or teaching of the desirability of making the specific combination that was made by the applicant. [Citations omitted].

In other words, "there still must be evidence that 'a skilled artisan, ... with no knowledge of the claimed invention, would select the elements from the cited

prior art references for combination in the manner claimed.'" Ecolochem Inc. v. Southern California Edison, 227 F.3d 1361, 1375, 56 USPQ2d 1065, 1075-76 (Fed. Cir. 2000). On this record, we find no evidence that a person of ordinary skill in the art, with no knowledge of appellants' claimed invention, would have selected the elements required to reach appellants' claimed invention from the genus of choices provided in Grande.

Accordingly, we reverse the rejection of claims 33-35, 40, 41, 43, 44, 47-49, 50 and 51 under 35 U.S.C. § 102(e) as being anticipated by or, in the alternative, under 35 U.S.C. § 103 as being obvious over Grande.

Claims 42, 45 and 46

Claims 42, and 45-46 stand rejected under 35 U.S.C. § 102(e) as anticipated by or, in the alternative, under 35 U.S.C. § 103 as obvious over Grande. Claim 42 depends ultimately from claim 33 and further requires that the cartilage defect comprises an articular cartilage injury, wherein the mesenchymal stem cells are administered through arthroscopic injection. Claim 45 depends from, and further limits, claim 44 to administering by injection directly into a synovial cavity in proximity to a lesion. Claim 46 depends from, and further limits, claim 44 the liquid suspension to further comprise serum or buffered saline.

To reach these additional limitations, the examiner finds a new set of inherent disclosures in Grande. Specifically, the examiner finds (Answer, page 5), "it is deemed inherent in the disclosure of the treatment of cartilage defects that the phrase [sic] 'injection', as used in the [Grande] patent, encompasses any

type of injection including injection made through an arthroscope, thereby anticipating the claim." The examiner also finds (Answer, bridging sentence, pages 5-6), Grande's "disclosure of treatment of … joints is deemed to inherently disclose an injection into the synovial cavity of these joints, thereby anticipating the claim." In addition, the examiner finds (Answer, page 6), Grande's "disclosure is deemed to inherently disclose a conventional pharmaceutical ingredient, phosphate buffered saline (PBS), thereby anticipating the claims."

Without reaching the merits of this new list of "inherent disclosures," we find it sufficient to state, this rejection suffers from the same deficiency as was discussed above with regard to claims 33-35, 40, 41, 43, 44, 47-49, 50 and 51. Accordingly, we reverse the rejection of claims 42, 45 and 46 under 35 U.S.C. § 102(e) as anticipated by or, in the alternative, under 35 U.S.C. § 103 as obvious over Grande.

THE REJECTIONS UNDER 35 U.S.C. § 103:

Claims 36 and 37

According to the examiner (Answer, page 7), "[c]laim 36 recites the further administration of a chondrogenesis promoting factor, specifically TGF-3 in [c]laim 37." While not expressly stated by the examiner, Grande does not teach this subject matter. To make up for this deficiency in Grande, the examiner relies on Bruder and Joyce. Id.

Bruder and Joyce, however, fail to make up for the deficiency in Grande. See supra. Accordingly, we reverse the rejection of claims 36 and 37 under 35 U.S.C. § 103 as being unpatentable over Grande in view of Joyce and Bruder.

Claim 38

According to the examiner (Answer, page 7), "[c]laim 38 recites the further administration of inhibitors of IL-1." While not expressly stated by the examiner, Grande does not teach this subject matter. To make up for this deficiency in Grande, the examiner relies on Bruder and Pettipher. Answer, pages 7-8.

Bruder and Pettipher, however, fail to make up for the deficiency in Grande. See supra. Accordingly, we reverse the rejection of claim 38 under 35 U.S.C. § 103 as being unpatentable over Grande in view of Bruder and Pettipher.

Claim 39

According to the examiner (Answer, page 7), "[c]laim 39 recites the further administration of inhibitors of osteochondral precursor cells." While not expressly stated by the examiner, Grande does not teach this subject matter. To make up for this deficiency in Grande, the examiner relies on Nevo and Itay. Answer, pages 7-8.

Nevo and Itay, however, fail to make up for the deficiency in Grande. See supra. Accordingly, we reverse the rejection of claim 39 under 35 U.S.C. § 103 as being unpatentable over Grande in view of Nevo and Itay.

SUMMARY

All rejections of record are reversed.

REVERSED

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Toni R. Scheiner	)
Administrative Patent Judge	)
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	)
	) BOARD OF PATENT
Donald E. Adams	)
Administrative Patent Judge	) APPEALS AND
	)
	) INTERFERENCES
	)
Demetra J. Mills	)
Administrative Patent Judge	)

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